

Diagnostic Approach to Polyarticular Joint Pain

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Identifying the cause of polyarticular joint pain can be difficult because of the extensive differential diagnosis. A thorough history and a complete physical examination are essential. Six clinical factors are helpful in narrowing the possible causes: disease chronology, inflammation, distribution, extra-articular manifestations, disease course, and patient demographics. Patients with an inflammatory arthritis are more likely to have palpable synovitis and morning stiffness; if the condition is severe, they may have fever, weight loss, and fatigue. Viral infections, crystal-induced arthritis, and serum sickness reactions are common causes of acute, self-limited polyarthritis. Because chronic arthritides may present abruptly, they need to be considered in patients who present with acute polyarticular joint pain. Joint palpation can help to distinguish inflammatory synovitis from the bony hypertrophy and crepitus that typically occur with osteoarthritis. Extra-articular manifestations of rheumatologic disease may be helpful in arriving at a more specific diagnosis. Many classic rheumatologic laboratory tests are non-specific. A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues. Plain-film radiographs may demonstrate classic findings of specific rheumatologic diseases; however, radiographs can be normal or only show nonspecific changes early in the disease process. (Am Fam Physician 2003;68:1151-60. Copyright© 2003 American Academy of Family Physicians.)

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Polyarticular joint pain (i.e., pain in more than four joints) poses a diagnostic challenge because of the extensive differential diagnosis¹ (Table 1). Consequently, family physicians need to keep the diagnosis open in evaluating patients who present with pain in multiple joints. For instance, a 50-year-old woman with symmetric, progressive polyarticular joint swelling and prolonged morning stiffness would seem to have rheumatoid arthritis. However, this patient might develop a malar rash and oral ulcers, which would change the diagnosis to systemic lupus erythematosus. Alternatively, the patient might develop thickening of the skin, which would suggest the diagnosis of scleroderma. Thus, a series of visits over time may be necessary to arrive at a specific diagnosis in many patients with polyarticular joint pain. In some patients, it may not be possible to establish a definitive diagnosis.

Because many rheumatologic laboratory tests lack the desired specificity, results should be interpreted in the clinical context and with caution. Tests with low specificity, such as those in arthritis panels, are frequently positive in the general population. Thus, these tests may be misleading.² Furthermore, use of

tests with low specificity may increase unnecessary testing and attendant costs, result in inappropriate treatment, and have a negative psychologic impact on patients.³

In the absence of definitive rheumatologic laboratory tests, the history and physical examination are key to the early diagnosis and treatment of conditions that cause polyarticular joint pain. Indeed, the differential diagnosis can be narrowed through investigation of six clinical factors: disease chronology, inflammation, distribution, extra-articular manifestations, disease course, and patient demographics (Table 2). More common causes of polyarticular joint pain should be considered first.

Disease Chronology

Acute polyarticular joint pain (i.e., pain that has been present for less than six weeks) may be the sign of a self-limited disorder or a harbinger of chronic disease. Although chronic polyarticular arthritides more often develop insidiously, they can present abruptly. Thus, chronic conditions such as rheumatoid arthritis and systemic lupus erythematosus should be considered, at least initially, in patients who present with acute polyarticular joint pain (Table 3).⁴⁻⁷ To avoid treating a self-limited

See page 1039 for definitions of strength-of-evidence levels.

TABLE 1
Differential Diagnosis of Polyarticular Joint Pain

Viral infection: human parvovirus (especially B19), enterovirus, adenovirus, Epstein-Barr, coxsackievirus (A9, B2, B3, B4, B6), cytomegalovirus, rubella, mumps, hepatitis B, varicella-zoster virus (human herpes virus 3), human immunodeficiency virus

Indirect bacterial infection (reactive arthritis): *Neisseria gonorrhoeae* (gonorrhea), bacterial endocarditis, *Campylobacter* species, *Chlamydia* species, *Salmonella* species, *Shigella* species, *Yersinia* species, *Tropheryma whippelii* (Whipple's disease), group A streptococci (rheumatic fever)

Direct bacterial infection: *N. gonorrhoeae*, *Staphylococcus aureus*, gram-negative bacilli, bacterial endocarditis

Other infections: *Borrelia burgdorferi* (Lyme disease), *Mycobacterium tuberculosis* (tuberculosis), fungi

Crystal-induced synovitis: gout, pseudogout (calcium pyrophosphate deposition disease), hydroxyapatite

Systemic rheumatic disease: rheumatoid arthritis, systemic lupus erythematosus, polymyositis/dermatomyositis, juvenile rheumatoid arthritis, scleroderma, Sjögren's syndrome, Behçet's syndrome, polymyalgia rheumatica

Systemic vasculitis disease: Schönlein-Henoch purpura, hypersensitivity vasculitis, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis

Spondyloarthropathies: ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, reactive arthritis (Reiter's syndrome)

Endocrine disorders: hyperparathyroidism, hyperthyroidism, hypothyroidism

Malignancy: metastatic cancer, multiple myeloma

Others: osteoarthritis, hypermobility syndromes, sarcoidosis, fibromyalgia, osteomalacia, Sweet's syndrome, serum sickness

TABLE 2
Common Causes of Polyarticular Joint Pain

Common causes of arthritis							
Disease	Chronology	Inflammation	Distribution			Extra-articular manifestations	Female-to-male ratio
			Pattern	Symmetry	Axial involvement		
Human parvovirus B19 infection	Acute	Yes	Small joints	Yes	No	Lacy rash, malar rash	3:1 to 4:1
Rheumatoid arthritis	Chronic	Yes	Small and large joints	Yes	Cervical	Subcutaneous nodules, carpal tunnel syndrome	3:1 to 4:1
Systemic lupus erythematosus	Chronic	Yes	Small joints	Yes	No	Malar rash, oral ulcers, serositis (pleuritis or pericarditis)	9:1
Osteoarthritis	Chronic	No	Lower extremity joints, proximal and distal interphalangeal joints, first carpometacarpal joint	Yes/No	Cervical and lumbar	None	1:1 to 2:1
Fibromyalgia	Chronic	No	Diffuse	Yes	Yes	Myalgias, tender points, irritable bowel syndrome	9:1
Ankylosing spondylitis	Chronic	Yes	Large joints	Yes	Yes	Iritis, tendonitis, aortic insufficiency	1:1 to 1:5
Psoriatic arthritis	Chronic	Yes	Large and small joints	Yes/No	Yes/No	Psoriasis, dactylitis ("sausage digits"), tendonitis, onychodystrophy	1:1

TABLE 3

Diagnostic Criteria for Rheumatoid Arthritis, Systemic Lupus Erythematosus, and Fibromyalgia

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Palpation of joint capsules can help to distinguish inflammatory synovitis from the noninflammatory bony hypertrophy that often indicates osteoarthritis.

disorder with potentially toxic disease-modifying agents, synovitis should be present for six weeks before rheumatoid arthritis is diagnosed.⁴ [Evidence level C, consensus opinion]

Viruses (e.g., human parvovirus B19, hepatitis viruses), crystals, and serum sickness reactions are known causes of acute, self-limited polyarthritis. The specific cause of virus-induced arthritis is not always investigated; thus, the prevalence of viruses as the etiology of arthritis may be underestimated.⁸

Except for *Neisseria gonorrhoeae*, direct bacterial infections in joints seldom cause polyarthritis.⁹ Although typically oligoarticular, extra-articular bacterial infections may induce acute arthritis. Classic reactive arthritis, for example, is associated with enteric infections (*Salmonella*, *Shigella*, *Campylobacter*, or *Yersinia* species) and urogenital infections (*Chlamydia trachomatis*).

Early gout usually affects only one joint. However, this disease also should be considered in patients with acute polyarticular arthritis, particularly older women who are taking diuretics and have hypertrophy and degenerative changes of the distal interphalangeal (DIP) joints (Heberden's nodes) and proximal interphalangeal (PIP) joints (Bouchard's nodes).¹⁰

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Inflammation

Arthritis is joint pain with inflammation, whereas arthralgia is joint pain without inflammation. The patient who presents with psoriasis and knee pain in the absence of inflammation may have the dual diagnosis of psoriasis and osteoarthritis. However, the patient who also has inflammation probably has psoriatic arthritis, which may require more aggressive therapy. Inflammatory arthritides include infectious arthritis, gout, rheumatoid arthritis, systemic lupus erythematosus, and reactive arthritis.

Cardinal signs of inflammation include erythema, warmth, pain, and swelling. Patients with severe joint inflammation or systemic disease also may present with fatigue, weight loss, or fever.⁸ Morning stiffness lasting longer than one hour suggests underlying inflammation.¹ The duration of morning stiffness provides a useful guide to the extent of inflammation. For instance, morning stiffness associated with rheumatoid arthritis may last for hours.^{11,12}

Palpation of multiple joint capsules is important to look for soft tissue swelling and effusions that result in edema and influx of inflammatory cells into and around the synovium. Soft tissue swelling should be distinguished from noninflammatory bony hypertrophy, such as Heberden's and Bouchard's nodes, which often indicate osteoarthritis (*Figure 1*). Crepitus indicates the pres-

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FIGURE 1.

ence of irregularities of the articular cartilage, which most commonly are associated with osteoarthritis, injury, or previous inflammation.

Because findings can be subtle, it is important to palpate each hand joint. Although palpation often can identify synovitis, it may not detect inflammation of more proximal joints in, for example, elderly patients with polymyalgia rheumatica.¹³

Morning stiffness and a history of swelling suggest an inflammatory process but also are characteristic of fibromyalgia, a noninflammatory condition (Table 3).⁴⁻⁷ Typically, patients with fibromyalgia have a subjective sense of swelling but no objective signs of synovitis. Fibromyalgia is suggested by the presence of polyarticular joint pain without synovitis, along with myalgias and tender points.¹⁴

Distribution

PATTERN

The pattern of joint involvement provides diagnostic clues. For instance, osteoarthritis of the hand usually involves the DIP and PIP joints, but not the metacarpophalangeal (MCP) joints.¹⁵ Alternatively, rheumatoid arthritis of the hand most often involves the PIP and MCP joints, but not the DIP joints.^{4,15} Psoriatic arthritis, crystal-induced arthritis, and sarcoidosis may affect all of these joints. Hand synovitis is distinctly unusual in chronic Lyme disease.¹⁶

Spondyloarthropathies typically involve the larger joints of the lower extremities. Osteoarthritis tends to spare wrists, elbows, and ankles, unless there is a history of trauma, inflammation, or a metabolic disorder such as hemochromatosis.

Depending on the underlying cause, the pattern of arthritis may change over time. For example, the acute stage of Lyme disease may include polyarticular arthralgias, whereas the chronic phase may include oligoarthritis, primarily in the knees.¹⁷

SYMMETRY

Joint involvement tends to be symmetric in systemic diseases such as rheumatoid arthritis, systemic lupus erythematosus, polymyalgia rheumatica, viral arthritides, and serum sickness reactions. Of eight variables examined in one study,¹⁸ symmetric pain was the most potent discriminating feature for rheumatoid arthritis. Psoriatic arthritis, reactive arthritis, and gout are more likely to present with asymmetric peripheral involvement.^{1,19,20}

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AXIAL INVOLVEMENT

Axial pain may be a helpful indicator in the evaluation of peripheral joint pain. In addition to peripheral joints, osteoarthritis may involve the lower back, the neck, or both. In contrast, rheumatoid arthritis is seldom an explanation for low back pain.

A young adult who presents with peripheral arthritis accompanied by the insidious onset of chronic low back pain and prolonged morning stiffness that improves with exercise probably has one of the spondyloarthropathies, such as ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease-associated arthropathy, or reactive arthritis.²¹ Another common manifestation of spondyloarthropathies is enthesitis (inflammation of the muscular or tendinous insertions),²² such as Achilles tendonitis or plantar fasciitis.²³ Dactylitis (inflammation of the finger or toe) is another classic sign of spondyloarthropathies; this condition, often referred to as "sausage digits," is caused by a combination of synovitis and enthesitis²² (Figure 2).

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FIGURE 2.

TABLE 4
Selected Extra-Articular Manifestations Associated with Conditions That Result in Polyarticular Joint Pain*

<i>Physical finding</i>	<i>Diagnoses to consider</i>	<i>Physical finding</i>	<i>Diagnoses to consider</i>
Skin and mucous membranes		Skin and mucous membranes continued.	
Rash		Telangiectasia	Scleroderma
Erythema infectiosum		Thickened skin	Scleroderma, amyloidosis, eosinophilic fasciitis
Reticulated (lacy) rash	Human parvovirus B19 infection	Hair thinning	Hypothyroidism, SLE
Facial exanthem (slapped cheek)	Human parvovirus B19 infection		
Malar rash	SLE, human parvovirus B19 infection, Lyme disease, rosacea, seborrhea, dermatomyositis	Musculoskeletal system	
Plaques (scalp, navel, gluteal cleft)	Psoriasis	Tender points	Fibromyalgia
Heliotrope	Dermatomyositis	Heberden's nodes (DIP joints), Bouchard's nodes (PIP joints)	Osteoarthritis
Erythema chronicum migrans	Lyme disease	Boutonnière and swan-neck deformities	RA, SLE, Ehlers-Danlos syndrome
Erythema marginatum rheumaticum	Rheumatic fever	Dactylitis ("sausage digits")	Spondyloarthropathies
Erythema nodosum	Sarcoidosis, Crohn's disease	Bursitis and enthesitis	Spondyloarthropathies
Pyoderma gangrenosum	IBD, RA, SLE, ankylosing spondylitis, sarcoidosis, Wegener's granulomatosis	Constitutional conditions	
Palpable purpura	Hypersensitivity vasculitis, Schönlein-Henoch purpura, PAN	Fever	Bacterial or viral infection, Still's disease, subacute bacterial endocarditis, neoplasm
Livedo reticularis	Antiphospholipid-antibody syndrome, vasculitis, cholesterol emboli	Bradycardia	Hypothyroidism
Lesions		Cardiovascular system	
Keratoderma blennorrhagicum	Reactive arthritis, psoriatic arthritis	Mitral regurgitation and stenosis	Rheumatic fever
Discoid skin lesions	Discoid lupus erythematosus, SLE, sarcoidosis	Aortic regurgitation	Ankylosing spondylitis, rheumatic fever, relapsing polychondritis, reactive arthritis, Marfan syndrome, Takayasu's arteritis
Gotttron's papules or plaques	Dermatomyositis	Cardiomyopathies	Viral infection, amyloidosis, sarcoidosis, SLE, polymyositis
Vesicopustule on erythematous base	Gonococcal arthritis	New murmur, fever	Bacterial endocarditis, rheumatic fever
Eyes		Diminished peripheral pulses	Giant cell arteritis, Takayasu's arteritis
Iritis or uveitis	Spondyloarthropathies, sarcoidosis, Wegener's granulomatosis	Gastrointestinal system	
Conjunctivitis	Spondyloarthropathies, SLE, Wegener's granulomatosis	Splenomegaly	Felty's syndrome, tumor-associated arthritis
Cytoid bodies (retinal exudates)	SLE	Hepatomegaly	Whipple's disease, hemochromatosis, amyloidosis, Wilson's disease
Scleritis	RA, relapsing polychondritis	Positive fecal occult blood test	IBD
Ischemic optic neuritis	Giant cell arteritis, Wegener's granulomatosis	Genitourinary system	
Ears, nose, and throat		Prostatitis	Reactive arthritis, ankylosing spondylitis
Oral ulcers	SLE, Behçet's syndrome, reactive arthritis, Wegener's granulomatosis	Urethritis or cervicitis	Reactive arthritis, gonococcal arthritis
Parotid enlargement	Sjögren's syndrome, sarcoidosis	Scrotal or vulvar ulcers	Behçet's syndrome
Macroglossia	Amyloidosis	Hypogonadism	Hemochromatosis
Scalp tenderness	Giant cell arteritis	Balanitis circinata	Reactive arthritis
Bloody or severe sinusitis	Wegener's granulomatosis	Neurologic system	
Inflammation of ear lobe	Relapsing polychondritis	Entrapment neuropathies	RA, hypothyroidism, hyperparathyroidism
Nails		Facial palsy	Lyme disease
Onycholysis	Psoriatic arthritis, hyperthyroidism	Peripheral neuropathy	SLE, amyloidosis
Pitting	Psoriatic arthritis	Chorea	Antiphospholipid-antibody syndrome, SLE, rheumatic fever
Clubbing	IBD, Whipple's disease, hyperthyroidism	Mononeuritis multiplex	RA, SLE, Lyme disease, vasculitis (e.g., PAN)
Nodules	RA, gout, Whipple's disease, rheumatic fever, amyloidosis, sarcoidosis	Seizures	SLE
Tophi	Gout	Lymphadenopathy	Tumor-associated arthritis, SLE
Jaundice	Hepatitis, hemochromatosis		
Hyperpigmentation	Whipple's disease, hemochromatosis		

SLE = systemic lupus erythematosus; IBD = inflammatory bowel disease; RA = rheumatoid arthritis; PAN = polyarteritis nodosa; DIP = distal interphalangeal; PIP = proximal interphalangeal.

*—The clues listed in this table are not, in themselves, diagnostic or complete; they are presented for illustrative purposes only.

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FIGURE 3.

Extra-Articular Manifestations

Extra-articular manifestations may provide clues to the presence of some rheumatologic diseases but, of themselves, are not diagnostic (*Table 4*). For instance, extra-articular signs and symptoms can point to the likely reason for swollen PIP joints: a malar rash and oral ulcers indicate probable systemic lupus erythematosus (*Figure 3*); proximal muscle weakness suggests polymyositis; and psoriatic skin and nail lesions raise the possibility of psoriatic arthritis.^{24,25}

Similarly, in a patient with knee arthritis, the presence of conjunctivitis, oral ulcers, vesicopustules on the soles, or recent diarrhea may indicate reactive arthritis.^{21,26} A history of erythema chronicum migrans and Bell's palsy points to the diagnosis of Lyme disease.²⁷ As a final example, a health care worker who presents with fever, a lacy rash, and symmetric joint pain (especially in the hands) may have erythema infectiosum caused by human parvovirus B19 infection.²⁸⁻³⁰

Disease Course

INTERMITTENT ARTHRITIS

When symptoms are present for a limited period (usually a few days to a month) and resolve completely before presenting again, crystal-induced arthritis (e.g., gout, pseudogout) is the likely diagnosis. Arthrocentesis should be considered during a symptomatic flare.^{10,19,27,31} If syn-

A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues than classic rheumatologic laboratory tests.

ovial fluid analysis fails to identify crystals, palindromic rheumatism should be considered; this condition may progress to rheumatoid arthritis.

MIGRATORY ARTHRITIS

Migratory arthritis is characterized by rapid onset of swelling in one or two joints, with resolution over a few days. As the symptoms resolve, similar symptoms emerge in another joint, usually in an asymmetric location.^{20,28} This symptom pattern can occur in gonococcal arthritis, rheumatic fever, sarcoidosis, systemic lupus erythematosus, Lyme disease, bacterial endocarditis, and Whipple's disease.³²

Patient Demographics

GENDER

Before menopause, women are nine times more likely to develop systemic lupus erythematosus and three to four times more likely to develop rheumatoid arthritis.²⁰ After men and women reach 50 years of age, the gender difference for systemic lupus erythematosus and rheumatoid arthritis becomes less significant.¹

Compared with men, women are nine times more likely to develop fibromyalgia. An estimated 60 percent of women with symptomatic human parvovirus B19 infection manifest arthropathy, whereas men with this infection appear to develop arthropathy much less often.^{33,34} The gender ratio is more balanced for spondyloarthropathies and vasculitic conditions such as polyarteritis nodosa.

Gout usually presents about 20 years after puberty in men and about 20 years after menopause in women. This disease is rare in premenopausal woman, unless renal insufficiency is present.¹⁰

AGE

Certain diagnoses are more common in specific age groups. Rheumatic fever, systemic lupus erythematosus, rheumatoid arthritis, reactive arthritis, and spondyloarthropathies occur more often in younger persons. Osteoarthritis, polymyalgia rheumatica, and giant cell arteritis are more common in older persons.¹³

TABLE 5
Findings of Laboratory and Imaging Tests and Associated Conditions That Result in Polyarticular Joint Pain

Laboratory or imaging test	Condition	Laboratory or imaging test	Condition
Complete blood count		Antinuclear antibody	Healthy persons; SLE, RA, scleroderma, Sjögren's syndrome, vasculitis, polymyositis, medications, many nonrheumatic causes
Anemia	Many inflammatory arthritides, especially SLE, RA, IBD, and human parvovirus B19 infection	Hepatic transaminase: elevated aspartate transaminase or alanine transaminase	SLE, PAN, sarcoidosis, hemochromatosis, Sjögren's syndrome, infectious hepatitis, polymyositis
Thrombocytopenia	SLE, human parvovirus B19 infection	Urinalysis	
Thrombocytosis	Acute-phase reaction, vasculitis, infection	Hematuria	SLE, Wegener's granulomatosis, PAN
Leukopenia	SLE, RA, Felty's syndrome, Sjögren's syndrome, human parvovirus B19 infection	Proteinuria	SLE; Wegener's granulomatosis, amyloidosis
Leukocytosis	RA, vasculitis, reactive arthritis, infection	Elevated alkaline phosphatase	Bone metastases, Paget's disease, osteomalacia, PMR, ankylosing spondylitis, hyperparathyroidism
Eosinophilia	SLE, RA, IBD, sarcoidosis, dermatomyositis, scleroderma, Churg-Strauss syndrome, PAN, eosinophilic fasciitis, cholesterol emboli	Electrocardiogram: atrioventricular block	Lyme disease, neonatal lupus, ankylosing spondylitis
Chest radiograph		Double-stranded DNA	SLE, especially lupus nephritis
Infiltrates or nodules	RA, sarcoidosis, Wegener's granulomatosis, Churg-Strauss syndrome	Anti-SS-A (anti-Ro) and anti-SS-B (anti-La) antibodies	Sjögren's syndrome, SLE; healthy persons
Serositis	SLE, RA	HLA-B27	Healthy persons; spondyloarthropathies, reactive arthritis
Upper lobe fibrosis	Ankylosing spondylitis	Elevated uric acid	Gout, psoriatic arthritis, Paget's disease; healthy persons
Diffuse fibrosis	RA, scleroderma, polymyositis	False-positive VDRL	SLE, anticardiolipin antibody syndrome
Rheumatoid factor	Healthy persons; RA, SLE, Sjögren's syndrome, sarcoidosis, reactive arthritis, PMR, polymyositis, psoriatic arthritis, endocarditis, chronic infections, cancer, chronic liver disease, many nonrheumatic causes	Cytoplasmic antineutrophil cytoplasmic autoantibody (c-ANCA)	Wegener's granulomatosis
Joint aspiration		Elevated creatinine	SLE, Wegener's granulomatosis, vasculitis
Culture	Infection	Elevated creatine kinase (CPK)	Polymyositis, dermatomyositis, hypothyroidism
Crystals	Gout, pseudogout	Elevated calcium	Hyperparathyroidism, cancer, sarcoidosis
White blood cell count	Inflammation: > 2,000 per mm ³ (2 × 10 ⁹ per L) Probable infection: > 50,000 per mm ³ (50 × 10 ⁹ per L)		
Inflammatory markers: elevated erythrocyte sedimentation rate or C-reactive protein (CRP)	Infection, most inflammatory arthritides, advanced age, PMR, giant cell arteritis, cancer, anemia, pregnancy; menses		

SLE = systemic lupus erythematosus; RA = rheumatoid arthritis; IBD = inflammatory bowel disease; PAN = polyarteritis nodosa; PMR = polymyalgia rheumatica.

RACE

Polymyalgia rheumatica and Wegener's granulomatosis are more likely to affect whites.¹³ In contrast, sarcoidosis and systemic lupus erythematosus are more common in blacks.

FAMILY HISTORY

Familial aggregation occurs in some arthritic diseases, such as spondyloarthropathies, rheumatoid arthritis, and

Heberden's nodes of osteoarthritis.¹ There is a particularly strong association between ankylosing spondylitis and the HLA-B27 allele.

Laboratory Investigations

As previously noted, many rheumatologic laboratory tests must be interpreted in the context of the individual patient. For example, antinuclear antibody (ANA) tests are positive in 5 to 10 percent of the general population, a rate

TABLE 6
Categorization of Synovial Fluid

Categorization	White blood cell count	Polymorphonuclear neutrophilic leukocytes	Examples
Normal	0 to 200 per mm ³ (0 to 0.2×10^9 per L)	<25% (0.25)	—
Noninflammatory	<2,000 per mm ³ (2×10^9 per L)	<25% (0.25)	Osteoarthritis, internal derangement, myxedema
Inflammatory	2,000 to 50,000 per mm ³ (2 to 50×10^9 per L)	>75% (0.75)	Rheumatoid arthritis, psoriatic arthritis, gout, pseudogout, <i>Neisseria gonorrhoeae</i> infection
Septic	>50,000 per mm ³ (50×10^9 per L); usually >100,000 per mm ³ (100×10^9 per L)	Usually >90% (0.90)	Septic arthritis (primary concern); occasionally, gout, pseudogout, reactive arthritis, Lyme disease

Information from reference 37.

that increases with age. Thus, given a one in 20 frequency for ANAs and a one in 2,000 frequency for systemic lupus erythematosus, only one in 100 persons with a positive ANA test will have the disease. Consequently, positive ANA test results must be interpreted with caution (Table 3).^{4,7} Given the high sensitivity of the currently used substrate for testing, a negative ANA test essentially rules out systemic lupus erythematosus.¹⁵

Spondyloarthropathies affect fewer than 1 percent of the general population. Indeed, patients who are HLA-B27 positive and do not have a family history of ankylosing spondylitis have only a 2 percent risk of developing this disorder.³⁵ Spondyloarthropathies can be overdiagnosed by relying only on a positive HLA-B27 test, because this test is positive in 8 percent of white persons.³⁵

Rheumatoid factor testing lacks both sensitivity and specificity: the test is positive in 5 to 10 percent of the general population and negative in approximately 20 percent of persons with rheumatoid arthritis.³⁶ Therefore, both positive and negative rheumatoid factor test results must be interpreted cautiously. Indeed, rheumatoid factor testing is not useful when a patient lacks other diagnostic criteria for rheumatoid arthritis, especially synovitis.³⁶ The American Rheumatology Association's revised diagnostic criteria for rheumatoid arthritis use findings from the history, physical examination, and laboratory tests.⁴ These criteria, which have been shown to be 91 to 94 percent sensitive and 89 percent specific, are useful for establishing a diagnosis of rheumatoid arthritis.^{4,12,15}

A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues than classic rheumatologic laboratory tests (Table 5). For instance, hematuria, proteinuria, a low white blood cell (WBC) count, and thrombocytopenia may indicate the presence of systemic lupus erythematosus. Anemia with a low mean corpuscular volume may be a sign of underlying inflammatory bowel disease that is causing chronic gastrointestinal

blood loss. Human parvovirus B19 infection can induce a decrease in the reticulocyte count, followed by anemia and, occasionally, leukopenia and thrombocytopenia.^{30,34}

Synovial fluid analysis is performed primarily to diagnose infection or a crystal-induced arthritis. A synovial fluid WBC count of at least 2,000 per mm³ (2×10^9 per L) suggests inflammation, whereas a count higher than 50,000 per mm³ (50×10^9 per L) typically indicates synovial infection (Table 6).³⁷ Fluid with a highly elevated WBC count or a predominance of neutrophils should be cultured to exclude infection.

Diagnostic Imaging

A number of radiographic findings are characteristic of specific rheumatic disorders. For instance, sacroiliitis is indicative of ankylosing spondylitis, erosions with periarticular osteopenia are typical of rheumatoid arthritis, and "pencil-in-cup" deformities are a sign of psoriatic arthritis. However, these radiographic findings take months to develop; early in the process, radiographs may be normal or show only nonspecific changes.

In early rheumatoid arthritis, magnetic resonance imaging demonstrates cartilage damage that is not evident on plain-film radiographs.³⁸ This damage highlights the importance of diagnosing rheumatoid arthritis early on the basis of the history and physical examination so that disease-modifying treatment can be initiated.

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